Docket No.: 05983/100J990-US1
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Adele L. Boskey et al.

Application No.: 10/603,478 Confirmation No.: 3518

Filed: June 24, 2003 Art Unit: 1614

For: COMPLEXED-ACIDIC-PHOSPHOLIPID-COLLAGEN COMPOSITES FOR BONE INDUCTION Examiner: B. Y. S. Kwon

DECLARATION OF ADELE L. BOSKEY, PH.D., UNDER 37 C.F.R. 1.132

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Adele L. Boskey, Ph.D., hereby declare:

1. I am one of the inventors of the above-referenced application

2. I am a professor at The Hospital for Special Surgery and in the Departments of Biochemistry and Physiology, Biophysics and Systems Biology, Cornell University Medical College in New York, New York.

3. I have reviewed the most recent office action by Examiner Kwan. Based upon this review, it is my understanding that the Examiner has concluded that a reference I authored in 1989 discloses and suggests a composition for osteoinduction which comprises a composite material comprising an acidic-phospholipid complex and collagen wherein the collagen is fibrillar and type I, type II or type IX or mixtures thereof. I respectfully disagree.

4. I am the sole author of the article in question "Hydroxyapatite Formation in a Dynamic Collagen Gel System: Effects of Type I Collagen, Lipids, and Proteoglycans" found in the Journal of Physical Chemistry (1989) 93:1628 (hereafter "Boskey").

5. In Boskey, I describe the hydroxyapatite formation in a gel system. As stated in Boskey, "[t]he purpose of the study was to develop a method for the study of hydroxyapatite formation and growth using a 'biologic matrix' in which the effect of agents believed to be involved in the control of calcification could be examined." Boskey, page 1628, right column, first paragraph.

6. The gels used for the study consisted of 10% wt of gelatin, which is denatured type I collagen. The gels were mounted on a device (as shown in Figure 1), and calcium and phosphate solutions were circulated at a continuous rate through the device, in separate loops at opposite ends of the gel. An "infinite reservoir" of calcium and phosphate were maintained during the experiments. Boskey, page 1628, right column, second and third paragraphs.

7. The gel system was used for the characterization of promoters and inhibitors of hydroxyapatite formation and growth by using well-characterized macro-molecules including complexed acidic phospholipids, fibrillar collagen, proteoglycan aggregates or monomer-containing fractions. See Boskey, abstract, page 1629, right column, forth and fifth paragraphs.

8. These four macro-molecules were never added to the gel at the same time. This is shown throughout Boskey, including the passages cited above where the conjunction "or" is used to describe the addition of the macro-molecules to the gel system. This is also shown by the results set forth in Tables II and III on page 1631 as well as the text describing the results, where the data for each macro-molecule added to the gel is set forth separately. For example, Boskey states "[t]he mineral ion contents of gels with and without fibrillar collagen were not significantly different, while gels with 1.2 mg/ml complexed acidic phospholipids had significantly more mineral ions than the control." These passages clearly show that Boskey does not disclose a gel system where the fibrillar collagen and the complexed acidic phospholipids are present at the same time. Thus, there is no disclosure in Boskey of a composition comprising complexed acidic phosholipids *and* fibrillar collagen, either complexed or not.

9. Additionally, the gel system described in Boskey contains gelatin. Gelatin is not the same substance as the type I, type II, and type IX collagen or mixtures thereof. Gelatin is water-soluble jelly-like protein produced either by heating or by partial hydrolysis of collagen. Because gelatin is denatured collagen, the natural molecular bonds between the individual collagen strands are broken down into a structural form that rearranges more easily. Gelatin has the distinguishing property of melting when heated, and solidifying when cooled again. It is used, for example, as a food additive, a pill coating, a base for ointments, and a biological substrate for cell culture. In contrast, collagen is the main protein of connective tissue in animals. Collagen is a long, fibrous structural protein and is the major component of connective tissue. Collagen consists of white inelastic fibers composed of fine fibrils, which themselves are composed of ever finer filaments, visible only with an electron microscope. Collagen molecules consist of three polypeptide chains coiled around each other to form a triple helix, stabilized by hydrogen bonds. Collagen is used for cosmetic surgery and treatment of burns. A person of skill in the art would not substitute collagen for gelatin and not believe that the use of one in a composition was interchangeable with the use of another.

10. In my opinion, Boskey does not teach or suggest a composition which comprises an acidic-phospholipids and type I, type II or type IX collagen or mixtures thereof. As stated above, these two components are never added to the gel at the same time. Additionally, gelatin is not the equivalent of fibrillar collagen. Moreover, Boskey reports that the gels containing the fibrillar collagen and those without did not have significantly different mineral ion content, where the gels with the acidic phospholipids had significantly more mineral ion content than the controls (Boskey, page 1631, Table II, and right column, first full paragraph). Boskey also reports other findings that fibrillar collagen does not promote calcium phosphate formation and is not a hydroxyapatite nucleator. See Boskey, page 1632, right column, second paragraph. This would suggest to a person of skill in the art that there would be no advantage to adding fibrillar collagen to a system to promote hydroxyapatite growth, only acidic phospholipids.

11. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States code, and that such willful false statements may jeopardize the validity of the instant application or of any patent issued thereupon.

Dated: 10/31/07

By: Adele L. Boskey

Adele L. Boskey, Ph.D.